REMARKS

Claims 4, 8, 15, 18, 21, and 47 – 68 are currently pending. Claim 55 is cancelled herewith and claims 65-68 are new. Claims 4, 8, 15, 50, 51, and 53 are currently amended.

Support for the amendment "at least two essential genes" to claim 4 can at least be found in original claim 55.

Support for the amendments to claims 4 and 8 can at least be found in para. [115], and [157] to [160] (for "one essential gene is an essential gene necessary for synthesis of the murein rigid cell wall layer, and one essential gene is an essential gene necessary for synthesis of diaminopimelic acid or is an essential gene necessary for synthesis of D-alanine") and in paras. [24] and [168] (for "wherein the essential genes are inactivated or operably linked to an activatable control sequence" and "wherein the essential genes of the vector complement the essential genes of the host chromosome that are inactivated or operably linked to an activatable control sequence"), all from the specification as originally filed.

Support for the amendment "wherein said vector further comprises a gene encoding a desired gene product" to claim 15 can at least be found in para. [3], [22], [25], and [26], all of the specification as originally filed.

Support for new claims 65 and 66 can at least be found in para. [29] of the specification as originally filed.

Support for new claims 67 and 68 can at least be found in para. [151], [152], and [153].

RESTRICTION

Applicants acknowledge the withdrawal of the restriction between the Group II and Group IV claims and respectfully request examination of the Group IV claims 21, 57 – 60, 62, and 63 pursuant to withdrawal of that Restriction by the Office.

CLAIM OBJECTIONS

The objection to claim 53 is obviated by the amendment provide herewith that specifies "wherein the terminator sequence is the *rrfG* ~~rrFG~~ transcriptional terminator". Withdrawal of the objection is respectfully requested.

DOUBLE PATENTING REJECTIONS

The following groups of claims were rejected for alleged non-statutory obviousness-type double patenting as follows:

i) 4, 15, 18, 47-51, 54, 56, and 64 over certain claims of U.S. Patent 6,610,529;

ii) 4, 15, 18, 21, 47-51, 56-60, and 62-64 over certain claims of U.S. Patent 6,780,405; and,

iii) 4, 15, 18, 47-51, 56-61, and 62-64 over certain claims of U.S. Patent 7,341,860.

Notably, neither claim 8 nor claim 55 were rejected by the Office for alleged non-statutory obviousness-type double patenting over any claims of the cited U.S. Patents. Since claim 4 as currently amended and all claims that depend therefrom incorporate the limitations of claim 55 (i.e. "at least two essential genes") and other features, the non-statutory obviousness-type double

patenting rejections of the currently pending claim 4 and claims that depend therefrom is no longer applicable. Claim 8 and the claims that depend therefrom remain free of any non-statutory obviousness-type double patenting rejections. Applicants respectfully request that the non-statutory obviousness-type double patenting rejections of the currently pending claims be withdrawn.

REJECTIONS UNDER 35 USC §102

Claims 4, 15, 18, 21, 47-51, 54, and 56-60 were rejected under 35 U.S.C 102(b) for alleged anticipation by Curtiss et al. (WO 96/40947). As admitted by the Office in page 10 of the Office Action of July 8, 2010, Curtiss et al. do not teach a vector system comprising two essential genes as specified by the then pending claims 8 and 55. Since claim 4 as currently amended and all claims that depend therefrom incorporate the limitation "at least two essential genes" of claim 55, Curtiss et al. no longer anticipate claim 4 as currently amended and all claims that depend therefrom. The Office is therefore respectfully requested to withdraw the rejections of claims 4, 15, 18, 21, 47-51, 54, and 56-60 under 35 U.S.C 102(b) over Curtiss et al.

REJECTIONS UNDER 35 USC §103

The following groups of claims were rejected for alleged obviousness over various references as follows:

i) 4, 15, 18, 47-51, 54, 56-60, 62 and 63 were alleged to be obvious over Curtiss et al. (WO 96/40947) in view of Jenkins et al. (Poultry Science, 1991, 70: 539-547, Abstract);

ii) 4, 15, 18, 21, 47-54, and 56-61 were alleged to be obvious over Curtiss et al. (WO 96/40947) in view of both Guzman et al. (J.Bacteriol., 1995, 177: 4121-4130) and Reddy et al. (Proc. Natl. Acad. Sci. USA, 1985, 82, 5656-5660); and,

iii) 4, 15, 18, 47-51, 54, 56-60, and 64, were alleged to be obvious over Curtiss et al. (WO 96/40947) in view of Shizuya et al. (Proc. Natl. Acad. Sci. USA, 1992, 89: 8794-8797). Notably, neither claim 8 nor claim 55 were rejected by the Office for alleged obviousness in this particular set of obviousness rejections (i.e. items 11, 12, and 13, on pages 7-0 of the Office Action of July 8, 2010). Since claim 4 as currently amended and all claims that depend therefrom incorporate the limitation "at least two essential genes" of claim 55, claim 4 as currently amended and all claims that depend therefrom are no longer disclosed nor suggested by these combinations of references (i.e. items 11, 12, and 13, on pages 7-0 of the Office Action of July 8, 2010). As per the apparent admission of the Office, Curtiss et al. does not teach a vector system comprising two essential genes and this deficiency is not remedied by Jenkins et al., Guzman et al., Reddy et al., or Shizuya et al. that rendered then pending claims 8 or 55 obvious. Since the claims as currently amended specify two essential genes, these combinations of references apparently do not meet the necessary factual finding under the *Graham* inquiries "that the prior art included each element claimed, although not necessarily in a single prior art reference, with the only difference between the claimed invention and the prior art being the lack of actual combination of the elements in a single prior art reference" (*See* MPEP§2143 A. (1)). Furthermore, MPEP §2143.03 also notes that " (i)f an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious. In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)". The Office is therefore respectfully requested to withdraw the

rejections of claims 4, 15, 18, 21, 47-54, and 56-64 under 35 U.S.C 103 over Curtiss et al. in view of Jenkins et al., Curtiss et al. in view of both Guzman et al. and Reddy et al., and Curtiss et al. in view of Shizuya et al.

Claims 4, 8, 15, 18, 21, 47-51, and 54-60 were rejected under 35 U.S.C. §103 over Curtiss et al. (WO 96/40947) in view of Curtiss (US Patent 4,190,495) and Oeschger (U.S. Patent 4,337,314). The Office alleges that the feature of two essential genes is suggested by Curtiss and Oeschger et al. that is admitted by the Office to be absent from Curtiss et al.

In considering this obviousness rejection over Curtiss et al. in view of Curtiss and Oeschger et al., we return to the factual findings under the *Graham* inquiries. As noted in the recently published "Examination Guidelines Update: Developments in the Obviousness Inquiry After KSR v.Teleflex", "(i)t It remains Office policy that appropriate factual findings are required in order to apply the enumerated rationales properly" (see Fed. Reg. 75, No. 169, paragraph spanning p. 53644 and p. 53645, September 1, 2010). First, we note that the claims as currently amended specify "an essential gene necessary for synthesis of the murein rigid cell wall layer, and one essential gene is an essential gene necessary for synthesis of diaminopimelic acid or is an essential gene necessary for synthesis of D-alanine". In contrast, Curtiss teaches, amongst an extensive list of mutations affecting a wide variety of cellular functions, the combination of two mutations that <u>both</u> abolish synthesis of diaminopimelic acid (*dap* and *asd;* Col. 3, l.38-40; Col. 4, l. 21-26; l. 50-59). Curtiss does not teach an essential gene necessary for synthesis of the murein rigid cell wall layer nor an essential gene necessary for synthesis of D-alanine as specified by the claims as currently amended. Curtiss does not teach the combination of an essential gene necessary for synthesis of the murein rigid cell wall layer and an essential

gene necessary for synthesis of diaminopimelic acid or an essential gene necessary for synthesis of D-alanine as currently claimed. Consistent with the teaching of two mutations that both affect synthesis of diaminopimelic acid, Curtiss also teaches that "two mutations affecting the same function are desirably employed whenever possible to preclude or greatly diminish the probability or possibility that the strain can lose the property conferred by such mutation or mutations" (*See* Col. 2, l. 24-30). As such, Curtiss effectively teaches away from the invention as currently claimed that specifies "an essential gene necessary for synthesis of the murein rigid cell wall layer, and one essential gene is an essential gene necessary for synthesis of diaminopimelic acid or is an essential gene necessary for synthesis of D-alanine". More specifically, Curtiss teaches that both mutations should be in the same function, such as two mutations that both abolish synthesis of diaminopimelic acid. Curtiss thus effectively teach away from combining a mutation in the function of synthesis of the murein rigid cell wall layer with the distinct functions of synthesis of diaminopimelic acid or synthesis of D-alanine as specified by the claims as currently amended. The deficiencies of Curtiss are not remedied by Oeschger et al. Like Curtiss et al., Oeschger et al. also does not teach an essential gene necessary for synthesis of the murein rigid cell wall layer nor an essential gene necessary for synthesis of D-alanine as specified by the claims as currently amended. Oeschger et al., in addition to disclosing a wide variety of auxotrophic mutations and mutations conferring resistance to selection agents, disclose mutations that can not synthesize diaminopimelic acid (DAP; *see* column 8, l. 12-20). Like Curtiss, Oeschger et al. do not teach the combination of an essential gene necessary for synthesis of the murein rigid cell wall layer and an essential gene necessary for synthesis of diaminopimelic acid or an essential gene necessary for synthesis of D-alanine as currently

claimed. Furthermore, Oeschger et al. also emphatically teach that "(t)he most important element of the invention is that the microorganisms have *multiple mutations of the same phenotype* in the same strain" (Column 7, l. 23-25; *emphasis added*; also see Col. 8, l. 66-68*)*. Oeschger et al. thus encourages having mutations in two essential genes that yield the *same* phenotype (i.e. such as mutations in two genes selected from *dapA, dapB, dapC, dapD, dapE, dapF* and *asd* where each mutation alone causes DAP auxotrophy). Oeschger et al. discourage having mutations in two essential genes that have different phenotypes (i.e. such as a mutation one gene necessary for murein rigid cell wall layer synthesis and a mutation in a gene necessary for DAP synthesis or a mutation in a gene necessary for D-alanine synthesis) as currently claimed. Also, the primary Curtiss et al. reference does not teach an essential gene necessary for murein rigid cell wall synthesis or the combination of an essential gene necessary for synthesis of the murein rigid cell wall layer and an essential gene necessary for synthesis of diaminopimelic acid or an essential gene necessary for synthesis of D-alanine as currently claimed.

Curtiss et al. in view of Curtiss and Oeschger et al. thus fail to establish a *prima facie* case for obviousness of the invention as currently claimed since this combinations of references does not meet the necessary factual finding under the *Graham* inquiries "that the prior art included each element claimed, although not necessarily in a single prior art reference, with the only difference between the claimed invention and the prior art being the lack of actual combination of the elements in a single prior art reference" (*See* MPEP§2143 A. (1)). Furthermore, there is also evidence that Curtiss and Oeschger et al. would discourage use of mutations in distinct types of essential genes involved in cell wall biosynthesis as currently claimed (i.e. in "an essential gene necessary for synthesis of the murein rigid cell wall layer, an

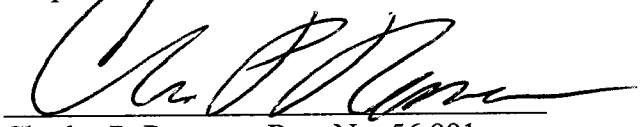
essential gene necessary for synthesis of diaminopimelic acid, or an essential gene necessary for synthesis of D-alanine"). The Office is therefore respectfully requested to withdraw rejections of the claims 4, 8, 15, 18, 21, 47-51, and 54-60 under 35 U.S.C 103 over Curtiss et al. in view of Curtiss and Oeschger et al.

CONCLUSION

We hereby petition for a two (2) month extension of time under 37 C.F.R. §1.136(a), and any fees required therefore are hereby authorized to be charged to our Deposit Account No. 20-0823. However, in the event that additional extension or other fees are necessary to prevent abandonment of this application, then such fees required are hereby authorized to be charged to our Deposit Account No. 20-0823.

The Examiner is encouraged to contact the undersigned via telephone at the number provided, if it is determined that personal communication will expedite prosecution of this application. The undersigned Agent hereby represents to the United States Patent and Trademark Office that he is authorized to represent the owners of this patent application pursuant to the provisions of 37 C.F.R. §1.34.

Respectfully submitted,



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